

### **REMARKS**

Claims 10 and 11 have been amended. Claims 12-17 have been canceled without prejudice. Claims 18-27 have been added. Support for the amendments and new claims can be found throughout the specification including the Drawings and claims as filed originally. No new matter has been added. Applicant appreciates the Examiner's acknowledgement of Applicant's claim for foreign priority based on an application filed in Denmark on January 23, 2001. A certified copy of the PA 2001 00118 application will be submitted under separate cover as soon as it is received from the Danish Patent Office. A new Declaration signed by the inventors will also be submitted under separate cover with claim for priority to provisional application 60/265,874 under 119(e) for domestic priority.

1. Claims 11-14 are objected to because of the following informalities:

The Examiner states with regard to claim 11, " The osteoclast bone disease "osteolytic cancer invation" is not familiar. The word "invation" should possibly be "invasion." Appropriate correction is required.

Claims 12-14 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim is dependent from another multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, claims 12-14 have been examined on the merits."

Claim 11 has been amended to correct the spelling error. Claims 12-17 have been canceled without prejudice, thereby obviating the objections.

2. Claims 13-15 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Dahl et al (WO 00/24707 as referenced in the IDS submitted February 13, 2004)

Claims 13-15 and 17 are drawn to treating an osteoclast related disorder using a chloride channel blocker of the CIC family.

Dahl et al teaches a method of using chloride channel blockers that are prepared as a medicament for the treatment of osteoclast disorders (page 9, lines 10-28, page 21, lines 30-35 bridging to page 22, lines 1-10, page 23, lines 15-20 and page 38). The chloride channel inhibitors disclosed in Dahl et al have the same intended use as claimed in the instant application and therefore inherently block the same chloride channels and treat that same osteoclast related bone diseases. Thus, Dahl et al teach all that is recited in the instant claims.

Claims 12-17 have been canceled without prejudice, thereby obviating the rejection.

3. Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner states, "Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, relative skill in the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claim, with the most relevant discussed below.

*Nature of the invention:* The claims are directed to a method of using identified compounds for the treatment, prevention and alleviation of osteoclast related bone disease that are chloride channel blockers of the CIC family.

*Breadth of the claim:* The claims are broad in that any identified or known compound can be used to block a

CIC chloride channel for treatment of any osteoclast related bone disease.

*Guidance in the specification/Existence of a working example:* The specification describes a screening method for identifying compounds that are potential blockers of the CIC chloride channel family. The specification indicates that any compound could be screened and that it is unpredictable which compounds that are identified will be useful as a therapeutic for osteoclast related bone disease. Furthermore, the specification does not describe any of the identified compounds or how to make any of the identified compounds.

In terms of the use of the compounds as therapeutics, the specification provides a working example for a screening method to identify compounds, but does not provide any working example or other evidence that an identified compound or blocker of CIC chloride channels are able to prevent the occurrence of an osteoclast related disease such as osteoporosis, osteolytic cancer, osteopetrosis or Paget's disease of bone in subject. Prevention requires a complete reversal of the disease state or complete inhibition of the occurrence of the disease state. *In vitro* data indicating that a compound was able to block a chloride channel does not predict the effect such a compound will have *in vivo* on the prevention of a variety of osteoclast disorders. Specifically, the specification has not taught an appropriate tested dose for each compound for each disease to be prevented in a subject, the number of times the treatment needs to be administered for each disease or the most appropriate route of administration. The lack of guidance in the specification would require trial and error experimentation to determine these factors.

*State of the art/Predictability of the art:* At the time of the applicants' invention, the general use of ion channel blockers in the treatment of various diseases was known. The specific use of CIC chloride channel blockers to prevent osteoclast disorders was not routine. Lark et al describes that the discovery of a role for CLC-7 chloride channel in the resorptive process in an osteoclast suggests that "CLC-7 potentially provides another excellent target for the inhibition of resorption" (Current Opinion in Pharmacology (2000), volume 2, pages 330-337, especially page 334, right column, second full paragraph). Several years after the time filing, the inventors demonstrate in an

osteoporosis animal model that complete prevention of osteoporosis is not possible by treating with a chloride channel inhibitor. Schaller et al demonstrates only partial protection of bone strength and BMD with one tested compound that may be inhibiting the CIC-7 chloride channel (Schaller et al. Journal of bone and mineral research: official journal of the American Society for Bone and Mineral Research (2004), volume 19 (7), pages 1144-1153, see especially abstract and page 1151). The lack of complete prevention demonstrates that one cannot predict the ability of any of the identified compounds or known chloride blockers to completely prevent osteoporosis or any other osteoclast related bone disease.

*Quantity of experimentation:* In order to practice the claimed invention, one of ordinary skill in the art would have to determine how to make all the identified compounds and determine their effectiveness in prevention of a osteoclast disorder *in vivo*. The skilled artisan would not be able to use the identified compounds or other CIC blockers as a therapeutic for the prevention of osteoclast related diseases without a large amount of trial and error experimentation to determine how to make and use the identified compounds in a treatment regimen.

*Conclusion:* In view of the unpredictable nature of the art, the lack of direction in the specification and the enormous amount of experimentation needed to make and use identified compounds, the experimentation would have been undue. Thus, it would require undue and unpredictable experimentation for one of skill in the art to perform the claimed invention. Therefore, the claimed invention of using an identified CIC chloride channel blocker to treat or prevent an osteoclast related disease is not considered to be fully enabled by the instant specification."

Claims 13-17 have been canceled without prejudice, thereby obviating the rejection.

4. Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states, "Claims 9 and 10 are drawn to a method of screening chemical compounds as potential therapeutics for an osteoclast related bone disease by testing the compounds on cells comprising chloride channels of CIC-3, CIC-6, CIC-7 and functional analogues thereof.

The specification does not describe all the functional analogues of the CIC-3, CIC-6 or CIC-7 chloride channels that would function in the method of screening compounds for the ability to treat, prevent or alleviate osteoclast related bone diseases. The specification merely describes that analogues can have "substantially equivalent activity" and include splice variants, isoforms and homologues from other species. The prior art does not offset the lack of description in the specification in that it does not describe functional analogues of these CIC chloride channels that would be useful targets for compounds in the treatment, prevention or alleviation of osteoclast related bone diseases. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of skill in the art to envision all the analogues of CIC-3, CIC-6 or CIC-7 that would possess the same function. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 9 and 10.

Claim 10 has been amended to delete any reference to "functional analogues thereof having substantially equivalent activity to the native forms, thereby obviating the basis for rejection. Applicant respectfully requests reconsideration.

5. Claims 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states, "The specification does not describe all the compounds or all the prodrugs or products of these compounds that function as chloride channel blockers of the CIC family for an osteoclast related bone disease therapy. The specification merely describes that chloride channel blockers of the CIC family and derivatives of these compounds in the form of prodrugs can be used to treat, prevent or alleviate an osteoclast related bone disease. The prior art does not offset the lack of description in the specification in that it does not describe all the derivatives of all the drugs that could function as a chloride channel blocker of the CIC family in the treatment of an osteoclast disorder. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of skill in the art to envision all the prodrugs or products of all the drugs that may function as a chloride channel blocker of the CIC family. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 13 and 15."

Claims 13 and 15 have been canceled without prejudice, thereby obviating the rejection.

6. Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states, "The specification does not describe any of the compounds that will be produced by the screening method for inhibitors of the CIC family or any compounds that function as chloride channel blockers of the CIC family. The specification merely describes that blockers of the CIC family of chloride channels can be used

in the treatment, prevention or alleviation of an osteoclast related bone disease without describing the compounds to be used for the treatment. The prior art does not offset the lack of description in the specification in that it does not describe all the potential compounds that will be produced and used in the treatment of the osteoclast related bone disease. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of skill in the art to envision all the compounds that would be used in the treatment of the osteoclast disorders. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 13-17.

Claims 13, 14 and 16 provide for the use of a blocker of a chloride channel of the CIC family, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced."

Claims 13-17 have been canceled without prejudice, thereby obviating the rejection.

7. Claims 13, 14 and 16 are rejected under 35 U.S.C. 101.

The Examiner states, "..... because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 13-17 have been canceled without prejudice, thereby obviating the rejection.

8. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states, "The metes and bounds of the claimed subject matter are not defined. It is unclear what is meant by "functional analogue" since it does not define the scope of the limitations.

Claim 10 has been amended to delete any reference to "functional analogues thereof having substantially equivalent activity to the native forms, thereby obviating the basis for rejection. Applicant respectfully requests reconsideration.

9. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner States, " A drug development method" is vague. What is meant by a drug development method since the limitations of the claim are already set forth in claims 9-11?

Claim 12 has been canceled without prejudice, thereby obviating the rejection.

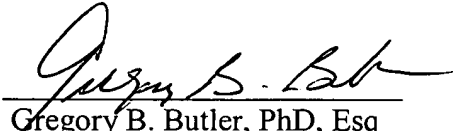
Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. Applicant's representative would like to discuss this case with the Examiner to learn if any outstanding issues remain after consideration of this Amendment. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call



the undersigned attorney of record. Should it be required, the Applicants conditionally petition for a extension of time to provide for the possibility that such a petition has been inadvertently overlooked and is required. As provided below, charge Deposit Account No. **04-1105** for any required fee.

Respectfully submitted,

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